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EXAMINER

SAIDHA, TEKCHAND

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/17/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 10/018730Applicant(s) Wong et al.Examiner T. SaidhaGroup Art Unit 165215

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P r i d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE —3— MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 11/15/02
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disp sition of Claims

- ☒ Claim(s) 20-37 is/are pending in the application.
- Of the above claim(s) 29-34 & 36-37 is/are withdrawn from consideration.
- ☐ Claim(s) is/are allowed.
- ☒ Claim(s) 20-28 & 35 is/are rejected.
- ☐ Claim(s) is/are objected to.
- ☐ Claim(s) are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

- ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ ☐ Interview Summary, PTO-413
- ☒ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other _____

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DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652.

2. ***Election***

Applicant's election of Group I (claims 20-28 & 35) in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 29-34 & 36-37 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 13.

3. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Great Britain on 06.18.99.

4. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

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5. Applicants' Preliminary Amendment filed April 4, 2002, is acknowledged. As per this amendment original claims 1-19 were canceled. New claims 1-18 presented were renumbered as per the rule 1.126.

6. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims **1-18** have been renumbered claims **20-37** respectively. The dependencies of the claims is also renumbered to match the corresponding renumbered claims. **Please make a note.** Applicants 'clean copy of claims' presented refer to the new claim numbers 20-28 & 35, but the numbering of the claim dependencies is in error.

7. ***Claim Rejections - 35 U.S.C. § 112*** (first paragraph)

Written Description

Claims 20-28 & 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 20-28 & 35 are drawn to a process for oxidizing any 'halo aromatic substrate' with one or more halogen atoms, and oxidizing the substrate using a monooxygenase from any source

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(claim 20-28 & 35); or where the enzyme is substituted by one or more amino acid(s) in the active site (claims 21-22); or where the enzyme is P-450cam or its naturally occurring homolog or mutant (claim 23, 28); or where amino acid 96 in one is substituted for another (claim 24); or where the halogen is chlorine (claim 25); or where the aromatic compound is benzene or biphenyl (claim 26); or specific substrate, example, 1, 2-dichlorobenzene (claim 27); and where the monooxygenase can be used to decontaminate any halo aromatic substrate by contacting with the enzyme, or with a transformed cell or non-human transgenic animal or transgenic plant capable of expressing the enzyme (claim 35).

The specification, however, only provides a single representative species of a process of oxidizing halo aromatic substrate, such as 1, 2-dichlorobenzene, ...hexachlorobenzene (see claim 27) using the monooxygenase from *Pseudomonas putida* of SEQ ID NO : 2 and the mutants based thereof. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species or modify the enzyme by substitution of one or amino acid(s) in the active site or make mutant monooxygenases by modifying any monooxygenase from any source. No description of any naturally occurring homologs of P-450cam is evident, and position 96 corresponding to which SEQ ID NO : ? remains undescribed. The specification does not define a “naturally occurring homolog”, which may be considered as an alternative form of the gene which may result in at least one mutation in the nucleic acid sequence. “Naturally occurring homolog” may be defined as a result in altered mRNAs or polypeptides whose structure or function may or may not

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be altered. Even such a definition does not provide any specific information about the structure of naturally occurring homolog of SEQ ID NO:2 (i.e. where is the likely regions within which mutations are likely to occur) nor discloses any function for naturally occurring homologs. There is no description of the mutational sites that exist in nature, and there is not description of how the structure of SEQ ID NO:2 relates to the structure of any naturally occurring homologs. The general knowledge in the art concerning homologs dose not provide any indication of how one homolog is representative of unknown homologs. Further it remains undescribed how the contaminated 'locus' [or surface] can be treated by contacting an enzyme, a transformed cell or by a transgenic animal (non-human) or plant. No such decontaminating formulations are described. The specification also fails to describe additional representative species of these monooxygenases or substrates other than those presented in claim 27, for example, by any identifying structural characteristics such as the properties or activity recited in claims, for which no predictability of structure is apparent. Given this lack of additional representative species, such as those discussed above, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

8. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claims 20-28 & 35 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 20, 27 & 35 recite the phrase 'halo aromatic substrate'. The claims are indefinite

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for it is not clear what the abbreviation 'halo' stand for. Is it 'halogen' or 'halogenated' ? Use of the complete word will overcome this rejection.

Claims 21-26 & 28 are included in the rejection for failing to correct the defect present in the base claim(s).

9. Claim 35, lines 1-2, recites method of treating a 'locus'. The dictionary meaning of 'locus' is : (a) locality : place & (b) the position that a gene occupies on a chromosome. The claim is indefinite because it is not clear what 'place' or 'position....' is being treated for contamination, and how a cell expresses (a)-(c). Is this a recombinant (transformed ?) Cell. Further it is very unclear how the contaminated 'locus' [or surface] can be treated by contacting with an enzyme, or a transformed cell or by a transgenic animal (non-human) or plant.

10. Claims 1 & 27 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (lines 3-4) after ... 'oxidizing said substrate with a monooxygenase enzyme', ...add.....an electron transfer reductase; and an electron transfer redoxin.....

11. ***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

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skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 20-28 & 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/14419 [Flitsch et al.] or US Patent 6,100,074 [Flitsch et al., same as WO 96/14419] and Shimoji et al. [Biochemistry (1998), 37, 8848-52].

Flitsch et al. [WO 96/14419] teach a number of specific mutants of mono-oxygenase P-450cam, including position 96 (Y96F mutant) of *Pseudomonas putida* wherein the ring carbon of the substrate is oxidized. Other mutational positions where one or more amino acids are modified in the active site include 87, 98, 101, 185, 193, 244, 147, 295, 297, 395 & 396 (see pages 2, 4 & 11) or by replacing 96Y by a less polar side chain (pages 3 & 4). The reference further teaches the gene and the encoding monooxygenase. The reference also suggests a method of oxidizing halo aromatic compounds, for example, diphenyl and biphenyl compounds and their halogenated variants (see page 4, lines 10-27 and claims 5 & 9). Assay mixture also contained electron transfer reductase; and an electron transfer redoxin. Flitsch et al. Also teach how to modify the active site of the wild type monooxygenase in order to decrease its specificity towards camphor, creating a desired 'aromatic pocket' (see pages 3 and 4) which would encourage binding of aromatic side chain (see page 2, 2nd paragraph).

Flitsch et al. do not teach oxidation of specific halo aromatic compounds (or one having more than one halogen molecule) or suggest using the enzyme in a process for oxidizing such halo aromatic compounds.

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Shimoji et al. suggests using modified P450 enzymes for the bioremediation of areas polluted with halo aromatic compounds. The assay shows the conversion of 4-chlorotoluene to 4-chlorobenzyl alcohol. [see pages 8849-50 & abstract].

Gooch et al. [Toxicology and Applied Pharmacology (1989) 98, 422-433] describe a number of specific polychlorinated biphenyl (PCBs) and the use of monooxygenase P-450 system for oxidations of these substrates.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the established method of Flitsch, wherein the mono-oxygenase (or mutants thereof) P-450cam system oxidizes a variety of well known substrates described therein, or substitute these substrates with the suggested (Shimoji et al.) halo aromatic substrates for the bioremediation or treatment of a surface contaminated with these compounds. In the alternative the suggested halo aromatic substrates for the bioremediation may include a polychlorinated biphenyl described by Gooch et al. With the mono-oxygenase P-450cam system well defined the use of the system for the oxidation of a variety of substrates including the PCBs or other well known halo aromatic substrates is well within the skill of an ordinary artisan, and can be achieved with a reasonable expectation of success. With the gene well known it would have been obvious to selectively express the mono-oxygenase, or transform a cell capable of expressing the mono-oxygenase or develop a non-human transgenic animal or transgenic plant whose cell expresses mono-oxygenase enzyme, electron transfer reductase; and an electron transfer redoxin, and do so with a reasonable expectation of success.

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One of ordinary skill in the art would have been motivated to develop such a process or treatment method in view of the well established importance of such methods in the use of the enzyme as catalysts for bioremediation of areas polluted with halo aromatic compounds, and such a suggestion is offered in the works of Shimoji et al. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, *prima facie* obvious.

12. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 20-24 are rejected under the judicially created doctrine of double patenting over claim 8 of U. S. Patent No. 6,100,074 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Claim 8 of USP 6,100,074 is drawn to a method of oxidising a compound which in the

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broadest sense will read upon 'halo aromatic compound', using a mono-oxygenase cytochrome P-450cam system, under oxidizing conditions. Claims 20-24 of the instant patent are anticipated by the cited patent.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Tekchand Saidha
Primary Examiner, Art Unit 1652
January 16, 2003